DEPARTMENT OF HEALTH & HUMAN SERVICES

P05 P940005

Public Health Service

Memorandum

Date APR 11 1996

From Director, Office of Device Evaluation (HFZ-400)
Center for Devices and Radiological Health (CDRH)

Subject Premarket Approval of Advanced Technology Laboratories Ultramark® 9 High Definition™ Imaging (HDI™) Ultrasound System and L10-5 Scanhead - ACTION

To The Director, CDRH
ORA _____

ISSUE. Publication of a notice announcing approval of the subject PMA.

FACTS. Tab A contains a FEDERAL REGISTER notice announcing:

(1) a premarket approval order for the above referenced medical device (Tab B); and

(2) the availability of a summary of safety and effectiveness data for the device (Tab C).

RECOMMENDATION. I recommend that the notice be signed and published.

Susan Alpert, Ph.D., M.D.

Attachments
Tab A - Notice
Tab B - Order
Tab C - S & E Summary

DECISION

Approved _____ Disapproved _____ Date _____

Prepared by Paul M. Gammell, CDRH, HFZ-470, March 18, 1996, 594-1212

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

DRAFT

[DOCKET NO. _____]

Advanced Technology Laboratories; PREMARKET APPROVAL OF Ultramark® 9 High Definition™ Imaging (HDI™) Ultrasound System with L10-5 Scanhead

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing its approval of the application by Advanced Technology Laboratories, Bothell, WA, for premarket approval, under the Federal Food, Drug, and Cosmetic Act (the act), of Ultramark® 9 High Definition™ Imaging (HDI™) Ultrasound System and L10-5 Scanhead. After reviewing the recommendation of the Radiological Devices Panel, FDA's Center for Devices and Radiological Health (CDRH) notified the applicant, by letter on April 11, 1996, of the approval of the application. DATES: Petitions for administrative review by (insert date 30 days after date of publication in the FEDERAL REGISTER).

ADDRESSES: Written requests for copies of the summary of safety and effectiveness data and petitions for administrative review, to the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Drive, Rm. 1-23, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT:

Robert Phillips,
Center for Devices and Radiological Health (HFZ-470),
Food and Drug Administration,
9200 Corporate Blvd.,
Rockville, MD 20850,
301-594-1212.

SUPPLEMENTARY INFORMATION: On February 17, 1994, Advanced Technology Laboratories, Bothell, WA 98041-3003, submitted to CDRH an application for premarket approval of the Ultramark® 9 High Definition™ Imaging (HDI™) Ultrasound System with L10-5 Scanhead. The device is an Ultrasonic Pulse-Echo Imaging System. The ATL Ultramark® 9 High Definition™ Imaging (HDI™) Ultrasound System with L10-5 Scanhead is indicated as an adjunct to mammography and physical breast examination to provide a high degree of physician confidence in differentiating benign from malignant or suspicious breast lesions. This device provides the physician with additional information to guide a biopsy decision. Utility of this system has been demonstrated for lesions with an indeterminate Level of Suspicion (LOS 2-4) by conventional diagnostic modalities. Using the HDI system in the evaluation of solid mass characteristics can reduce the number of biopsies performed on indeterminate lesions.

On December 11, 1995, the Radiological Devices Panel, an FDA advisory committee, reviewed and recommended approval of the application.

On April 11, 1996, CDRH approved the application by a letter to the applicant from the Director of the Office of Device Evaluation, CDRH. A summary of the safety and effectiveness data on which CDRH based its approval is on file in the Dockets Management Branch (address above) and is available from that office upon written request. Requests should be identified with the name of the device and the docket number found in brackets in the heading of this document.

Opportunity for Administrative Review

Section 515(d)(3) of the act (21 U.S.C. 360e(d)(3)) authorizes any interested person to petition, under section 515(g) of the act, for administrative review of CDRH's decision to approve this application. A petitioner may request either a formal hearing under part 12 (21 CFR part 12) of FDA's administrative practices and procedures regulations or a review of the application and CDRH's action by an independent advisory committee of experts. A petition is to be in the form of a petition for reconsideration under 10.33(b) (21 CFR 10.33(b)). A petitioner shall identify the form of review requested (hearing or independent advisory committee) and shall submit with the petition supporting data and information showing that there is a genuine and substantial issue of material fact for resolution through administrative review. After reviewing the petition, FDA will decide whether to grant or deny the petition and will publish a notice of its decision in the FEDERAL REGISTER. If FDA grants the petition, the notice will state the issue to be reviewed, the form of the review to be used, the persons who may participate in the review, the time and place where the review will occur, and other details.

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Petitioners may, at any time on or before (insert date 30 days after date of publication in the FEDERAL REGISTER), file with the Dockets Management Branch (address above) two copies of each petition and supporting data and information, identified with the name of the device and the docket number found in brackets in the heading of this document. Received petitions may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

This notice is issued under the Federal Food, Drug, and Cosmetic Act (secs. 515(d), 520(h), (21 U.S.C. 360e(d), 360j(h))) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.10) and redelegated to the Director, Center for Devices and Radiological Health (21 CFR 5.53).

Dated: _____.

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
1390 Piccard Drive
Rockville MD 20850

Terrence J. Sweeney
Director, Worldwide Regulatory Affairs
Advanced Technology Laboratories
22100 Bothell Everett Highway
Post Office Box 3003
Bothell, Washington 98041-3003

APR 11 1996

Re: P940005
Ultramark® 9 High Definition™ Imaging (HDI™) Ultrasound System with L10-5 Scanhead
Filed: February 17, 1994
Amended: June 20, 1994 and February 16, July 17, August 28, October 10, 20, and 30, November 6 and 7, December 18 and 29, 1995, February 20 and 23, March 4, 11, 13, 19, and 26, and April 11, 1996.

Dear Mr. Sweeney:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the Ultramark® 9 High Definition™ Imaging (HDI™) Ultrasound System with L10-5 Scanhead.

The ATL Ultramark® 9 High Definition™ Imaging (HDI™) Ultrasound System with L10-5 Scanhead is indicated, as an adjunct to mammography and physical breast examination, to provide a high degree of physician confidence in differentiating benign from malignant or suspicious breast lesions. This device provides the physician with additional information to guide a biopsy decision. Utility of this system has been demonstrated for lesions with an indeterminate Level of Suspicion (LOS 2-4) by conventional diagnostic modalities. Using the HDI system in the evaluation of solid mass characteristics can reduce the number of biopsies performed on indeterminate lesions.

We are pleased to inform you that the PMA is approved subject to the conditions described below and in the "Conditions of Approval" (enclosed). You may begin commercial distribution of the device upon receipt of this letter.

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that to ensure the safe and effective use of the device that the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii), (1) insofar as the labeling must specify the requirements that apply to the training of practitioners who may use the device as approved

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in this order and (2) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

CDRH will publish a notice of its decision to approve your PMA in the FEDERAL REGISTER. The notice will state that a summary of the safety and effectiveness data upon which the approval is based is available to the public upon request. Within 30 days of publication of the notice of approval in the FEDERAL REGISTER, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the act.

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

You are reminded that as soon as possible, and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

If you have any questions concerning this approval order, please contact Paul M. Gammell, Ph.D. at (301) 594-1212.

Sincerely yours,

Susan Alpert, Ph.D., M.D.
Director
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

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Issued: 5-2-95

CONDITIONS OF APPROVAL

APPROVED LABELING. As soon as possible, and before commercial distribution of your device, submit three copies of an amendment to this PMA submission with copies of all approved labeling in final printed form to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration (FDA), 9200 Corporate Blvd., Rockville, Maryland 20850.

ADVERTISEMENT. No advertisement or other descriptive printed material issued by the applicant or private label distributor with respect to this device shall recommend or imply that the device may be used for any use that is not included in the FDA approved labeling for the device. If the FDA approval order has restricted the sale, distribution and use of the device to prescription use in accordance with 21 CFR 801.109 and specified that this restriction is being imposed in accordance with the provisions of section 520(e) of the act under the authority of section 515(d)(1)(B)(ii) of the act, all advertisements and other descriptive printed material issued by the applicant or distributor with respect to the device shall include a brief statement of the intended uses of the device and relevant warnings, precautions, side effects and contraindications.

PREMARKET APPROVAL APPLICATION (PMA) SUPPLEMENT. Before making any change affecting the safety or effectiveness of the device, submit a PMA supplement for review and approval by FDA unless the change is of a type for which a "Special PMA Supplement-Changes Being Effected" is permitted under 21 CFR 814.39(d) or an alternate submission is permitted in accordance with 21 CFR 814.39(e). A PMA supplement or alternate submission shall comply with applicable requirements under 21 CFR 814.39 of the final rule for Premarket Approval of Medical Devices.

All situations which require a PMA supplement cannot be briefly summarized, please consult the PMA regulation for further guidance. The guidance provided below is only for several key instances.

A PMA supplement must be submitted when unanticipated adverse effects, increases in the incidence of anticipated adverse effects, or device failures necessitate a labeling, manufacturing, or device modification.

A PMA supplement must be submitted if the device is to be modified and the modified device should be subjected to animal or laboratory or clinical testing designed to determine if the modified device remains safe and effective.

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A "Special PMA Supplement - Changes Being Effected" is limited to the labeling, quality control and manufacturing process changes specified under 21 CFR 814.39(d)(2). It allows for the **addition** of, but **not the replacement** of previously approved, quality control specifications and test methods. These changes may be implemented before FDA approval upon acknowledgment by FDA that the submission is being processed as a "Special PMA Supplement - Changes Being Effected." This acknowledgment is in addition to that issued by the PMA Document Mail Center for all PMA supplements submitted. **This procedure is not applicable to changes in device design, composition, specifications, circuitry, software or energy source.**

Alternate submissions permitted under 21 CFR 814.39(e) apply to changes that otherwise require approval of a PMA supplement before implementation of the change and include the use of a 30-day PMA supplement or annual postapproval report. FDA must have previously indicated in an advisory opinion to the affected industry or in correspondence with the applicant that the alternate submission is permitted for the change. Before such can occur, FDA and the PMA applicant(s) involved must agree upon any needed testing protocol, test results, reporting format, information to be reported, and the alternate submission to be used.

POSTAPPROVAL REPORTS. Continued approval of this PMA is contingent upon the submission of postapproval reports required under 21 CFR 814.84 at intervals of 1 year from the date of approval of the original PMA. Postapproval reports for supplements approved under the original PMA, if applicable, are to be included in the next and subsequent annual reports for the original PMA unless specified otherwise in the approval order for the PMA supplement. Two copies identified as "Annual Report" and bearing the applicable PMA reference number are to be submitted to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850. The postapproval report shall indicate the beginning and ending date of the period covered by the report and shall include the following information required by 21 CFR 814.84:

(1) Identification of changes described in 21 CFR 814.39(a) and changes required to be reported to FDA under 21 CFR 814.39(b).

(2) Bibliography and summary of the following information not previously submitted as part of the PMA and that is known to or reasonably should be known to the applicant:

(a) unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices ("related" devices include devices which are the same or substantially similar to the applicant's device); and

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(b) reports in the scientific literature concerning the device.

If, after reviewing the bibliography and summary, FDA concludes that agency review of one or more of the above reports is required, the applicant shall submit two copies of each identified report when so notified by FDA.

ADVERSE REACTION AND DEVICE DEFECT REPORTING. As provided by 21 CFR 814.82(a)(9), FDA has determined that in order to provide continued reasonable assurance of the safety and effectiveness of the device, the applicant shall submit 3 copies of a written report identified, as applicable, as an "Adverse Reaction Report" or "Device Defect Report" to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850 within 10 days after the applicant receives or has knowledge of information concerning:

(1) A mixup of the device or its labeling with another article.

(2) Any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and

(a) has not been addressed by the device's labeling or

(b) has been addressed by the device's labeling, but is occurring with unexpected severity or frequency.

(3) Any significant chemical, physical or other change or deterioration in the device or any failure of the device to meet the specifications established in the approved PMA that could not cause or contribute to death or serious injury but are not correctable by adjustments or other maintenance procedures described in the approved labeling. The report shall include a discussion of the applicant's assessment of the change, deterioration or failure and any proposed or implemented corrective action by the applicant. When such events are correctable by adjustments or other maintenance procedures described in the approved labeling, all such events known to the applicant shall be included in the Annual Report described under "Postapproval Reports" above unless specified otherwise in the conditions of approval to this PMA. This postapproval report shall appropriately categorize these events and include the number of reported and otherwise known instances of each category during the reporting period. Additional information regarding the events discussed above shall be submitted by the applicant when determined by FDA to be necessary to provide continued reasonable assurance of the safety and effectiveness of the device for its intended use.

REPORTING UNDER THE MEDICAL DEVICE REPORTING (MDR) REGULATION. The Medical Device Reporting (MDR) Regulation became effective on December 13, 1984, and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to FDA whenever they receive or otherwise became aware of information that reasonably suggests that one of its marketed devices

(1) may have caused or contributed to a death or serious injury or

(2) has malfunctioned and that the device or any other device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

The same events subject to reporting under the MDR Regulation may also be subject to the above "Adverse Reaction and Device Defect Reporting" requirements in the "Conditions of Approval" for this PMA. FDA has determined that such duplicative reporting is unnecessary. Whenever an event involving a device is subject to reporting under both the MDR Regulation and the "Conditions of Approval" for this PMA, you shall submit the appropriate reports required by the MDR Regulation and identified with the PMA reference number to the following office:

Division of Surveillance Systems (HFZ-531)
Center for Devices and Radiological Health
Food and Drug Administration
1350 Piccard Drive, Room 240
Rockville, Maryland 20850
Telephone (301) 594-2735

Events included in periodic reports to the PMA that have also been reported under the MDR Regulation must be so identified in the periodic report to the PMA to prevent duplicative entry into FDA information systems.

Copies of the MDR Regulation and an FDA publication entitled, "An Overview of the Medical Device Reporting Regulation," are available by written request to the address below or by telephoning 1-800-638-2041.

Division of Small Manufacturers Assistance (HFZ-220)
Center for Devices and Radiological Health
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

ATL Breast Lesion Sonography Study PMA

Summary of Safety and Effectiveness Data

I. GENERAL INFORMATION

Device generic name:	Ultrasonic pulsed Doppler imaging system and diagnostic ultrasonic scanhead
Device trade name:	Ultramark® 9 High Definition™ Imaging (HDI™) Ultrasound System with L10-5 Scanhead
Applicant's name:	Advanced Technology Laboratories 22100 Bothell Everett Highway Post Office Box 3003 Bothell, Washington 98041-3003

PMA number: P940005

Date of panel recommendation: December 11, 1995

Date of notice of approval to the applicant: APR 11 1996

II. INDICATIONS FOR USE

The ATL Ultramark® 9 High Definition™ Imaging (HDI™) Ultrasound System with L10-5 Scanhead is indicated as an adjunct to mammography and physical breast examination to provide a high degree of physician confidence in differentiating benign from malignant or suspicious breast lesions. This device provides the physician with additional information to guide a biopsy decision. Utility of this system has been demonstrated for lesions with an indeterminate Level of Suspicion (LOS 2-4) by conventional diagnostic modalities. Using the HDI system in the evaluation of solid mass characteristics can reduce the number of biopsies performed on indeterminate lesions.

III. DEVICE DESCRIPTION

The ATL Ultramark® 9 High Definition™ Imaging (HDI™) Ultrasound System with L10-5 Scanhead is a general purpose diagnostic ultrasound system that has received 510(k) marketing clearance by K903603 and K903627. For this indication the device consists of the L10-5, 192-element, 5-10 MHz broadband, 38-mm flat linear array scanhead together with electronic and mechanical hardware, including digital components, comprising the ultrasound system console. The Ultramark® (HDI™) Ultrasound System is sold as part numbers 8500-0010 and 8500-0011. It is operated by proprietary software. The L10-5 Scanhead is sold as part numbers 8500-8168 and 8500-8280. This is the only scanhead used for this indication.

The maximum acoustic outputs for the breast scanning modes are: $I_{SPTA.3}$=682 mW/cm^2, $I_{SPPA.3}$=306 W/cm^2, and MI=1.2. The ATL Ultramark® 9 High Definition™ Imaging (HDI™) Ultrasound System and L10-5 are used in the following modes for the breast lesion sonography indication: 2D imaging, pulsed Doppler, and color Doppler.

IV. CONTRAINDICATIONS, WARNINGS, AND PRECAUTIONS

CONTRAINDICATIONS

There are no contraindications.

WARNINGS

The ATL-HDI Breast protocol does not replace normal screening methods for detecting breast disease by mammography or palpation, and evaluation using biopsy when appropriate.

The mass seen on the ultrasound examination and the mass seen on the mammographic examination may not be the same mass; orientation must be carefully checked, especially when performing a biopsy on one of several lesions.

If a mass cannot be visualized when attempting to follow the HDI protocol, then no change in prior levels of suspicion should be made.

Overlap in ultrasound image appearance between benign and malignant breast lesions does exist.

PRECAUTIONS

The attending physician should determine the applicability of HDI results and the need for biopsy based upon individual patient characteristics and history.

Proper use of ATL's device requires that training of Sonographers and Sonologists take place prior to use of the HDI system for breast lesion differentiation.

This device has not been demonstrated effective for masses less than 1.0 cm, as measured by mammography.

Semiannual quality checks to verify system performance should be performed.

To ensure optimal image evaluation there should be no prior surgical intervention of the breast, and at least two weeks healing should be allowed to occur following any percutaneous intervention of the breast.

V. ALTERNATE PRACTICES AND PROCEDURES

Other modalities used in the diagnostic evaluation of solid breast lesions are diagnostic mammography, duplex sonography, magnetic resonance imaging, nuclear medicine, computed tomography, digital mammography, incisional biopsy, fine needle biopsy, and core biopsy.

VI. MARKETING HISTORY

The HDI system was 510(k) cleared for marketing as a general purpose diagnostic ultrasound device, including breast sonography, through the premarket notification process (K903603 and K903627) in February 1991 for 2D imaging, pulsed and color flow Doppler. It has not been previously marketed for the indication for use which is the subject of this PMA (i.e., adjunctive to mammography for the evaluation of indeterminate lesions). It has not been withdrawn from any country for any reason related to safety or use.

VII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

No adverse effects were reported during premarket clinical trials.

There are several potential effects on the patient with respect to ultrasound in general that have been reported in the literature: (1) dermal reactions such as reddening or burning of the skin from excessive temperature due to a device failure that causes overheating of the transducer lens (2) tissue damage from an acoustic output control failure causing possible cavitational or thermal cell damage and (3) allergic reactions to the gel used to couple the scanhead to the skin.

VIII. NON-CLINICAL STUDIES

A. BIOCOMPATIBILITY

When used for this indication the ATL HDI system will have short-term contact with the intact skin, similar to that for which the device has previously received 510(k) clearance.

The patient contact materials are primarily the scanhead lens, which is made of RTV 700-136, and incidentally the scanhead housing, which is made of Udel P-1700. Biocompatibility testing was conducted by North American Science Associates, Inc. (NAmSA) in Irvine, CA. The tests conducted and the results are summarized in Table I.

Table I. Biocompatibility tests conducted on patient contacting components of L10-5 scanhead.

component	lens	body	discussion
material	RTV 700-136	Udel p-1700	
test	results	results	
Mucosal Irritation	passed	not tested	material extract to rabbit vagina
Primary Skin Irritation	passed	passed	intact and abraded skin of rabbits
Acute Systemic Toxicity	not tested	passed	inject mice with extract (saline, cotton seed oil)
Intracutaneous Toxicity	not tested	passed	injection of rabbits with extract (saline, cotton seed oil)

B. PHYSICAL ENVIRONMENTAL TESTING

The system is UL approved for electrical safety. The system is specified to operate over the range of -8.3% to +10% of the selected line voltage, which can be 100, 120, 220, or 240 volts; over a temperature range of 50 to 104°F; and over a humidity range of 15 to 95%. The scanhead successfully passed environmental, vibration, enclosure strength, temperature rise, cable pull, electrical safety, and drop stress testing.

C. CONTRAST-DETAIL PHANTOM TESTING

The performance characteristics that make the HDI system suitable for the indication for use include the ability to produce images of breast masses that have sufficient resolution to give the physician a high degree of confidence in deciding if a biopsy is necessary. To determine the smallest detail that the HDI system can resolve for the range of contrasts encountered in typical breast lesions, ATL conducted imaging tests using a custom contrast-resolution phantom.

Contrast-detail analysis[1,2,3] allows the measurement of the resolution limits of an ultrasound imaging system as a function of contrast. This test uses a contrast-detail (CD) phantom composed of tissue mimicking material (TMM) with embedded conical targets, also made of TMM, which range in contrast over a specified range. The contrast of the conical targets may be either positive (brighter than background) or negative (darker than background). Contrast-resolution capability is measured by imaging successively smaller cross-sections of the CD phantom targets, and identifying the target cross-section diameter at which the target image can no longer be differentiated from the background image.

Although there are published procedures for performing these tests, there is not a scientific consensus. Therefore only the clinical data were used to support the claim for resolution capability.

D. DOPPLER PERFORMANCE CHARACTERISTICS

The performance characteristics that allow the HDI system to perform the subject indication include its ability to visualize very small blood vessel physiological flow rates. The Roberts Research Institute (London, Ontario, Canada) conducted an independent study of the Doppler performance of the HDI system, using a specially designed flow phantom, using bovine blood, which emulates small vessel diameters, low flow rates, and vessel depths similar to those in the breast. These tests demonstrated that the HDI system successfully detects blood flow in vessels as small as 1.2 mm diameter, at depths of 1.5 to 5 cm, at flow velocities of 3, 16, and 29 cm/sec. These velocities were seen by ATL in clinical practice. These measurements were performed using the HDI "Breast" setup, using both color Doppler and spectral Doppler measurements of time-averaged mean velocity. These simulated vessel diameters were the smallest that could be built into the phantom, and the flow speeds were the lowest that could be duplicated. The 1.5 mm is representative of the smaller arteries found in the breast. It is not practical to represent the lower limit of the capillaries, which go down to around 10 microns.

E. QUALITY ASSURANCE

To insure that the HDI system does not degrade in performance, ATL developed a quality assurance protocol which allows the user to periodically insure that the quality of images is maintained. This assures that the system maintains its ability to discriminate benign from malignant characteristics for the specified range of sizes corresponding to the system's maximum capabilities.

F. ACOUSTIC OUTPUT TABLES

The maximum acoustic output power and intensity of the L10-5 scanhead is given in the Ultramark 9 HDI Reference Manual and listed in Table II below:

Table II. Acoustic output of the L10-5 scanhead for modes used in the breast ultrasound protocol.

Mode	Freq, MHz	Depth, cm	MI	I_{SPTA}, mW/cm^2		I_{SPPA}, W/cm^2		I max, W/cm^2	
				derated	water	derated	water	derated	water
2D	7.5	1.6	0.8	94	225	186	431	289	668
Pul Dop	6.0	1.9 1.7*	1.2	618	1342	279	553	289	571
2-D &PD	6.0	1.9 1.7*	1.2	682	1825	306	617	337	814
color 2D	6.0	1.9 1.7*	1.2	153	332	306	617	404	814

*Depth for the maximum MI, I_{SPPA} and intensity.

IX. CLINICAL STUDIES

A. OVERVIEW

A multi-site study was conducted to investigate the clinical utility of the ATL HDI system and L10-5 scanhead for the differentiation of benign and malignant breast lesions when used adjunctively to mammography and physical examination. This study compared the HDI ultrasound results and the radiologic results of suspect lesions with the gold standard of pathology results. Each of the subjects enrolled in the study had a previous suspicious finding resulting in a biopsy recommendation. Observations consisted of gathering HDI ultrasound data from subjects per the protocol. Investigators scored the level of suspicion (LOS) three times for each subject: pre-HDI mammographic/palpation, HDI 2D grey scale, and post-HDI Doppler results. A final diagnostic call that the mass was likely malignant or benign was then made by the investigator. This information was then compared to the pathology reports and ROC analysis and performance parameters results were calculated.

B. STUDY HYPOTHESIS:

The hypothesis of this study was that HDI ultrasound, using the Ultramark® 9 High Definition™ Imaging (HDI™) Ultrasound System with L10-5 Scanhead, when used adjunctively with mammography and physical exam for breast lesion assessment would result in a significant increase in specificity with at least the same level of sensitivity as has been demonstrated by standard diagnostic modalities. HDI ultrasound, when used adjunctively with mammography and physical exam would significantly reduce the biopsy rate when used on masses classified by mammography and physical exam as indeterminate LOS (Level of Suspicion). An intermediate LOS is 2, 3, or 4. A LOS of 1 was considered definitely benign and 5, definitely malignant.

C. DIAGNOSTIC CRITERIA FOR THIS INDICATION

The image criteria by which the HDI-2D and HDI-Doppler were interpreted are central to this new indication. The guidelines for interpretation of HDI-2D and HDI Doppler as provided in the in the labeling are as follows:

2D Image Criteria Guidelines for Differentiation of Solid Breast Lesions

Image Criteria Associated with Benign Lesions

1. Spherical/ovoid/lobulated shape
2. Linear margin
3. Homogeneous texture
4. Isoechoic/anechoic
5. Edge shadow
6. Parallel to the skin
7. Distal Enhancement
8. Dilated duct/mobile

Image Criteria Associated With Malignant Lesions

1. Irregular shape
2. Poorly defined margin
3. Central shadowing
4. Distorted architecture
5. Calcifications
6. Skin thickening

Doppler Criteria Guidelines for Differentiation of Solid Breast Lesions

Doppler Criteria Associated With Benign Lesions

1. Same or less global variance when compared to the contralateral breast.
2. Same or less vascularity when compared to the contralateral breast.

Doppler Criteria Associated With Malignant Lesions

1. More global variance when compared to the contralateral breast.
2. More vascularity when compared to the contralateral breast.

The assignment of a LOS based on HDI 2D Image should be based on the guidelines in Table III.

Table III. Assignment of LOS based on HDI-2D Image Criteria

HDI-2D LOS	Number of criteria observed	Assessment based on HDI-2D alone
5	5 malignant criteria	malignant
4	3-4 malignant criteria	probably malignant
3	1-2 malignant criteria	indeterminate
2	0 malignant criteria	probably benign
1	0 malignant criteria and all benign criteria	benign

In addition to the 2D imaging criteria, the Doppler attributes listed above can be used to help differentiate a mass. Specific guidelines were not developed for numerical evaluation of the Doppler criteria.

A final overall level of suspicion from both the HDI examination and conventional modalities enabled the attending physician to determine the need for biopsy based upon all available data. It is this overall level of

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suspicion, reflected in the physician's call that was recorded in the study protocol, that was used to assess the performance of this device as an adjunct to physical examination or mammography.

D. METHODS:

All subjects who were scheduled for a biopsy based upon their physicians' interpretations of clinical and family histories, mammography, and/or physical examination of breast lesions were eligible for inclusion into this study. The investigator determined a level of suspicion (LOS) for a lesion on a range of 1 to 5, with 1 being the lowest level of suspicion and 5 being the highest. The LOS was reported after each step in the patient work-up: after the biopsy referral from mammography and/or physical examination (pre-HDI), after the HDI system 2D scan (HDI-2D), and after the HDI system Doppler exam (post-HDI-Doppler). In addition, a diagnostic call (malignant or benign) was made by the investigator at the conclusion of the HDI study, blinded to the biopsy result. The biopsy result (surgical or core needle) was used as the definitive diagnosis; thus each patient served as her own control.

E. POPULATION:

Patients from nine U.S. and five non-U.S. sites entered into this study. This was a representative group of women who presented for diagnostic work-up or breast cancer screening and were recommended for breast biopsy. A total of 1270 patients, with 1334 masses were enrolled. Data from all patients who entered into this study were used to assess the safety of this device.

The analysis to determine the effectiveness of this device was based on a subset of the masses of these patients, which will be referred to as the Sub-Study Population. This is derived from the Study Population by excluding masses that did not meet specific study criteria.

First, masses were excluded from this population because they were

1) biopsied by FNA (Fine Needle Aspiration)
   (since FNA was not accepted as a "gold standard" for diagnosis),
2) not visualizable with HDI ultrasound (e.g., microcalcification),
3) were of less than 0.5 cm size, or
4) diagnosed as cystic upon completion of the pre-HDI work-up.

These four reasons, singly or in combination, accounted for the exiting of 295 masses and 275 patients. The exclusion of one international site, Freiburg, Germany (Site No. 09), because the protocol was not consistently followed, resulted in the exclusion of 203 additional masses and 196 patients. This resulted in a population of 799 patients with 846 masses.

Second, masses in the above population that had a pre-HDI LOS of 1 or 5 were excluded.

Exclusion of the 296 masses in 278 patients of the above population that had a pre-HDI LOS or 1 or 5 resulted in a population of 550 masses in 521 patients. This provided the data on a population of eligible masses with indeterminate LOS that was presented to the Panel.

Third, masses in the above population that were less than 1.0 cm in size were excluded.

Exclusion of the 119 masses, in 110 patients of the above population, that were less than 1.0 cm in size resulted in the final Sub-Study Population of 431 masses in 411 patients. The mass size was determined by mammography or by ultrasound (if a mammographic mass size was not available). This is the population upon which a determination of effectiveness was made. The number of patients and masses enrolled from each site and the number of each that were part of the Sub-Study Population are listed in Table IV.

Table IV. The number of patients and masses studied at each center.

		Study Population		Sub-Study Population	
		patients	masses	patients	masses
Center 1	West Penn	82	91	21	22
Center 2	Ochsner	117	118	47	48
Center 3	UAB	97	99	28	28
Center 4	Yale	206	229	110	123
Center 5	Cincinnati	95	100	29	30
Center 6	Loma Linda	53	58	15	15
Center 7	TJU	171	177	83	84
Center 8	M. D. Anderson	55	68	8	8
Center 9	Chicago	12	13	3	4
	U. S. Total	888	953	344	362
Center 10	Toronto	37	39	20	22
Center 11	Royal Marsden	13	13	7	7
Center 12	Freiburg	196	203	0	0
Center 13	Paris	105	105	29	29
Center 14	South Hampton	31	31	11	11
	Non-US Total	382	391	67	69
	Overall Total	1270	1344	411	431

F. DEMOGRAPHICS:

The 1270 women in the Study Group had a mean age of 51.0 years, a mean height of 64.4 inches, and a mean weight of 150.3 pounds. The majority of the patients were Caucasian (81.3%). Slightly over half of the women (54.6%) had reached menopause and 69.9% were from the United States.

The 411 women in the Sub-Study Group had a mean age of 48.3 years (range 20-89), a mean height of 64.3 inches (range 56-80), and a mean weight of 156.8 pounds (range 95-310). The majority of the patients were Caucasian (75.1%), 18.4% were black, 3/3% were Hispanic, 2.2% were Asian, 0.6% were Native American, and the remaining 6.0% other races. Slightly under half of the women (44.9%) had reached menopause and 78.3% were from the United States. The ethnic composition is representative of the United States population.

G. STUDY DURATION

The study was conducted between February 1992 and March 1994

H. EVALUATION OF SAFETY AND EFFECTIVENESS

1. SAFETY

All 1270 patients enrolled in the study that had an HDI ultrasound exam were used for evaluation of safety results. There were no reported thermal, dermal, allergic reactions or adverse events.

2. EFFECTIVENESS

a. STATISTICAL METHODS:

The primary statistical technique used to determine the effectiveness of this device was the receiver operating characteristic (ROC) analysis. This approach facilitates the comparison of devices over a range of sensitivities and specificities. The technique is explained by Metz[4] and Hanley[5]. The ROC curve for a given device, operator, or situation is generated by plotting the true positive fraction vs the false positive fraction as the threshold parameter (LOS in this case) is varied. The curves for two devices can be easily compared. If the curve for one device is higher for all threshold values, its performance is clearly superior regardless of the threshold parameter the operator chooses. The curves clarify the trade-offs if they cross. One parameter that is useful for quantifying the performance of a device is the area under the ROC curve. An area of 1.0 represents ideal performance: a 100% true positive can be reached with no false positive calls. Operation along the 45 degree line (false positive fraction equals true positive fraction) represents pure chance.

In this study the ROC analysis tables compared LOS results of mammography and physical examination (pre-HDI) versus the results of post-HDI-Doppler. The post-HDI-Doppler assessment used the cumulative information derived from mammography, physical examination and HDI 2D imaging (post-HDI-2D) or mammography, physical examination, HDI-2D imaging and HDI Doppler. Indices for area under the curve and sensitivity with specificity at 0.85 and 0.60 were evaluated for differences in pre-HDI and post-HDI-Doppler. The objective was to provide a 95% confidence interval of ±2%.

Standard performance parameters for sensitivity, specificity, positive predictive value and negative predictive values were also calculated and compared for statistical significance. Performance parameters were determined by comparing a test method's accuracy to a gold standard. The gold standard used was the biopsy result.

b. RESULTS

Effectiveness of this device was assessed based on the lesions of the Sub-Study Population of n=431 masses. ROC analysis was the primary tool by which effectiveness was assessed. The performance parameters were also provided. Analyses were also performed to determine if lesion size or patient age were factors that significantly limited performance.

An ROC analysis was conducted to compare three types of examinations: 1) mammography or physical examination alone (pre-HDI), 2) the combined results of mammography, physical exam and HDI ultrasound 2D imaging (post-HDI-2D), and 3) the combined results of mammography, physical exam and HDI ultrasound by both 2D imaging and Doppler (post-HDI-Doppler).
The ROC curves for these three types of examinations are shown in Figure 1. The ROC curve for mammography here is based on three categories: LOS=2, 3, 4, which the lesions in the Sub-Study Population had prior to the HDI examinations. The additional data from the HDI examination of these same lesions

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generated all five categories: LOS 1-5, upon which the ROC curves for post-HDI 2D and post-HDI Doppler were based.

Table V compares the three key parameters derived from these curves: the area under the curve, which is a measure of the overall performance, and the sensitivity at two fixed values of specificity. The last column of this table shows the 95% confidence interval for the difference of each parameter pre-HDI vs post-HDI-Doppler.

Table V: ROC Analysis Comparing pre-HDI LOS to Post-HDI-Doppler LOS for Indeterminate Masses 1.0 cm and Larger (n=431).

ROC Index	Pre-HDI	Post-HDI-Doppler	95% CI range (P-value)
Area under the ROC Curve	0.850	0.920	0.024-0.114 (0.0024)
Sensitivity at Spec = 0.85	0.664	0.828	0.053-0.275 (0.0037)
Sensitivity at Spec = 0.60	0.890	0.970	0.021-0.139 (0.0098)

The increase in area under the curve, sensitivity at a specificity of 0.85, and sensitivity at a specificity of 0.60 post-HDI-Doppler were highly statistically significant. The ROC comparison indicates that results post-HDI-Doppler are statistically significantly better than results following mammography and physical exam for all three indices when specifically evaluating the indeterminate population.

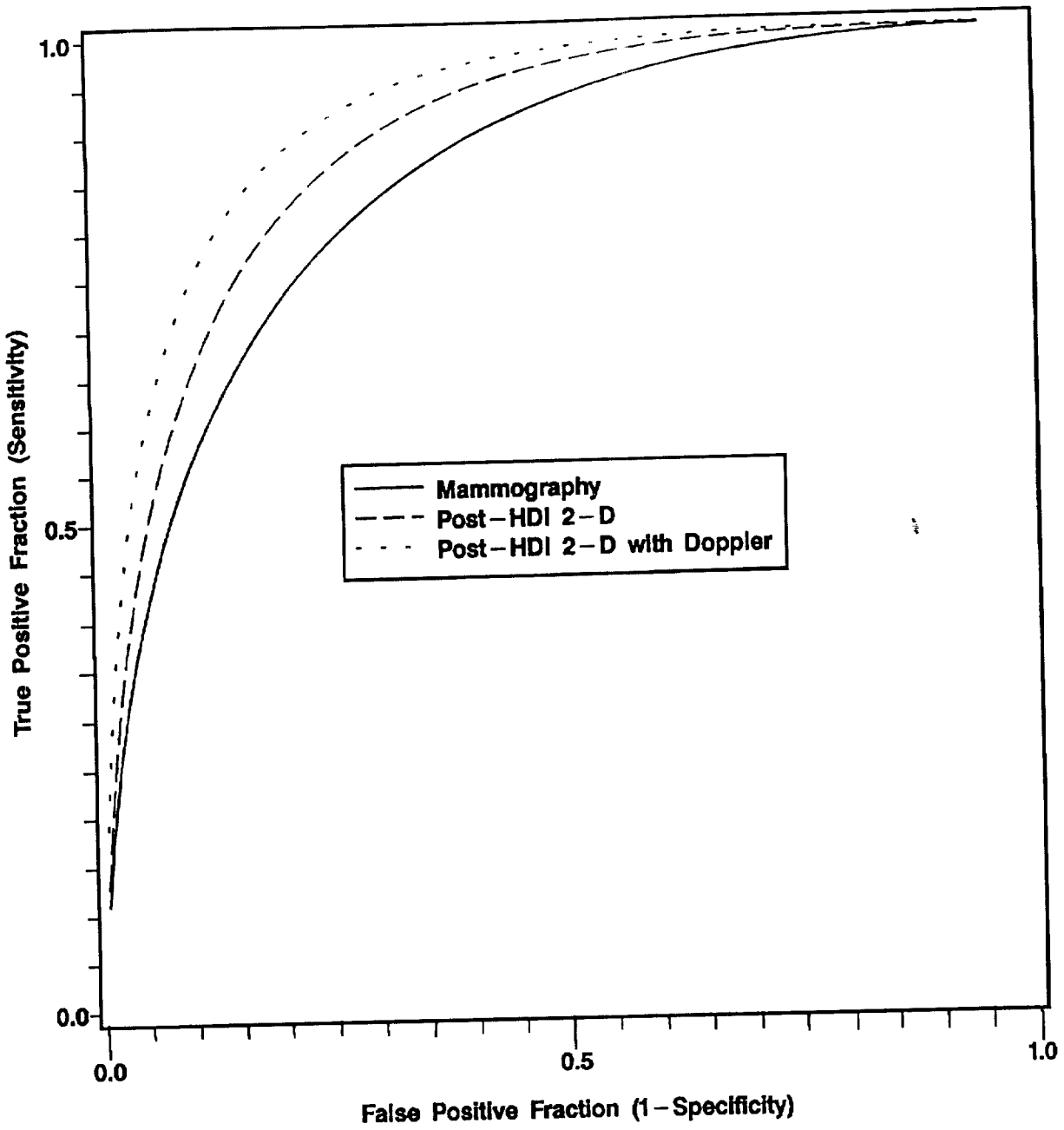

Figure 1. ROC curves comparing performance of mammography, HDI-2D, and HDI-Doppler for masses 1 cm and larger with a pre-HDI LOS of 2, 3, or 4 (n=431 masses).

Table VI presents the traditional performance parameters and their 95% confidence intervals for this same population. The performance parameters for pre-HDI were based on the cumulative LOS for the pre-HDI information (mammography and/or physical examination) alone. The performance parameters for post-HDI-Doppler are shown as calculated for the physician's call based on all available information. Each of the performance parameters increased in this subpopulation post-HDI-Doppler evaluation.

Table VI, Performance Parameters Comparing Mammography and Physical Exam to Post-HDI Doppler Results for lesions 1.0 cm and larger with an Indeterminate pre-HDI Result (LOS 2, 3, and 4).

Performance Parameter (Post-HDI-Doppler)	Pre-HDI (95% CI range)	Post-HDI-Doppler (95% CI range)
Performance based on:	LOS definition[†]	Physician's Call
Sensitivity	95.0 (90.6-99.3)	100.0 (96.3-100.0)
Specificity	44.3 (38.9-49.6)	53.0 (47.6-58.4)
PPV	33.7 (28.2-39.2)	38.8 (32.8-44.8)
NPV	96.7 (93.9-99.6)	100.0 (100.0-97.9)

c. PREDICTED REDUCTION OF BIOPSY RATE

The HDI breast ultrasound exam is applicable for lesions with a pre-HDI LOS of 2, 3 or 4 (based on mammography or physical examination and possibly conventional ultrasound). Lesions with a LOS of 5 are so suspicious that they would probably be biopsied anyway. Lesions with a pre-HDI LOS of 1 would not normally be biopsied, so any additional information would not reduce the biopsy rate. The data reported from this study were used to predict how much the use of HDI ultrasound could reduce the biopsy rate for lesions of at least 1.0 cm size which have a pre-HDI LOS of 2, 3, or 4. If the HDI results were used to determine the need for biopsy in the study 40.1% of the patients would not have received a biopsy, as shown in Table VII.

[†]Calculation of the performance parameters of sensitivity, specificity, PPV and NPV must be based on a dichotomous scale. Although a LOS was assigned both pre-HDI and post-HDI, the only physician's call required by the protocol was that based on the post-HDI information. Therefore calculation of the pre-HDI performance parameters required reducing the LOS to a dichotomous scale. This scale was derived by defining a LOS of 1 or 2 as a benign call and a LOS of 3, 4, or 5 as a malignant call.

Table VII. Reduction of the Biopsy Rate for Lesions 1.0 cm and Larger Which Have a Prior LOS of 2, 3, or 4.

Total number of indeterminate lesions	431
Lesions determined negative by HDI	176
Number of False Negatives by HDI	0
Reduction in biopsy rate, calculation	(176+0)/431
Reduction in biopsy rate, per cent	40.1%

d. ANALYSIS OF EFFECTIVENESS VS AGE

In Table VIII the results of a sub-analysis of the performance parameters by patient age are shown. Although the number of patients in most age groups are too small to assign high confidence, this data is intended to allow assessment substantial trends that may affect the applicability to the extreme age groups. These analyses were based on the Indeterminate Mass, Size-Restricted Population.

Table VIII. Performance Indicators Separated by Age for Lesions 1.0 cm and Larger Which Have a Prior LOS of 2, 3, or 4, With the Final Diagnosis Based on the Physician's Call.

Age, years	<20	21-30	31-40	41-50	51-60	61-70	>70
Sensitivity, calc.	0/0	3/3	13/13	16/16	24/24	19/19	18/18
Sensitivity, %	-----	100	100	100	100	100	100
Specificity, calc.	1/1	14/26	61/90	66/114	14/45	16/40	1/7
Specificity, %	100	53.8	67.8	57.9	31.1	40.0	14.3
PPV, calculation	0/0	3/15	13/42	16/64	24/55	19/43	18/24
PPV, %	---	20.0	31.0	25.0	43.6	44.2	75.0
NPV, calculation	1/1	14/14	61/61	66/66	14/14	16/16	1/1
NPV, %	100	100	100	100	100	100	100

The sensitivity and negative predictive value are seen to remain high for all age groups for which they are applicable. It should be noted that the prevalence is zero for the patients less than 20 years of age in this study, and thus the sensitivity and negative predictive value for that group are not determined by this study. The specificity shows an almost linear decrease from 75% for ages less than 20 years to 33% for ages greater than 70 years. The positive predictive value roughly tracks the prevalence, increasing from 31% for the 21-30 age range to 75% for the over 70 range, while the prevalence is increasing from 13% to 67% over the same age range. This data supports the performance for the ages of 21 years to over 70 years. The data neither support nor refute the performance for women under 20 years of age

e. ANALYSIS OF EFFECTIVENESS VS LESION SIZE

In table IX the performance parameters are analyzed for sub-populations of lesion sizes. The population analyzed here is a sub-set of the Study Population that meets all of the criteria of the Sub-Study Population except for the size limitation. All lesions 0.5 cm and larger that are not otherwise excluded from the Sub-Study Population are considered here. There is a total of 550 masses in this population, of which 449 have mass sizes recorded. This analysis is only intended to reveal gross trends and to determine the *minimum* lesion size for the labeling. The number of lesions in some of the groups is too small for analysis of subtle trends.

Table IX. Performance Parameters for 4 Ranges of Lesion Size, With the Final Diagnosis Based on the Physician's Call.

Mass size, cm.	<1.0	1.0-1.5	1.51-2.5	>2.5
number of masses	117	240	133	59
Sensitivity, calc.	30/30	54/54	37/37	9/9
Sensitivity, %	100.0	100.0	100.0	100.0
Specificity, calc.	45/87	96/186	55/96	25/50
Specificity, %	51.7	51.6	57.3	50.0
PPV, calculation	30/72	54/144	37/78	9/34
PPV, %	41.7	37.5	47.4	26.5
NPV, calculation	45/45	96/96	55/55	25/25
NPV, %	100.0	100.0	100.0	100.0

The sensitivity remains high for all ranges of lesion sizes in this table. Since the sensitivity and specificity remain high for the lesions of the smallest size range (< 1.0 cm), the effectiveness for the range above (1.0 to 1.5 cm) is supported. Detailed size analysis has not been conducted and no claim is being made for lesions less than 1.0 cm in diameter.

X. CONCLUSIONS DRAWN FROM THE STUDIES

The Center for Devices and Radiological Health reviewed all submitted nonclinical and clinical data. The clinical studies demonstrate that the ATL Ultramark® 9 High Definition™ Imaging (HDI™) Ultrasound System with L10-5 Scanhead can provide a high degree of physician confidence in differentiating benign from malignant or suspicious breast lesions that have been detected by mammography or physical examination. The data from the clinical studies suggest that using the HDI system in the evaluation of solid mass characteristics can reduce the number of biopsies performed on indeterminate lesions. The clinical studies provide reasonable assurance that this device is safe and effective for its labeled indication.

XI. PANEL RECOMMENDATION

A meeting of the FDA Radiological Devices Panel took place on December 11, 1995 to review the sponsor's submission, PMA 940005, as amended. The panel voted for approval under the following conditions:

1. The indication for use statement should be revised to the following: The HDI system is indicated to provide a high level of confidence in differentiating benign from malignant or suspicious lesions that have been detected by

mammography and/or physical examination for which diagnosis is indeterminate (LOS 2-4). Using the HDI system to evaluate solid mass characteristics can reduce the number of biopsies performed on indeterminate lesions as diagnosed by mammography or physical examination.

2. The lower lesion size approved for evaluation using the HDI system is 1 cm until the FDA receives data from the company providing a significant performance improvement using 2D-HDI for lesions less than 1 cm in size or if the company produces well defined Doppler criteria and reanalyzed their data to show a significant improvement using those Doppler criteria in conjunction with 2D HDI.

3. A training program for sonographers and sonologists should be developed and that the program be reviewed by FDA prior to implementation.

4. The percent reductions in biopsies stated in the labeling should be supported by appropriate data from the manufacturer.

XII. CDRH DECISION

CDRH concurred with the recommendation of the Panel. The panel recommendations were adopted with minor editing to reflect their intent, as shown in part II of this Summary of Safety and Effectiveness Data. In addition FDA has required ATL to submit a quality assurance program by which the user verify that the performance of the device remains adequate for the stated indication. Based on the clinical and nonclinical data submitted, CDRH approved the PMA for the stated indication on April 11, 1996.

The applicant's manufacturing and control facilities were inspected on February 8, 1996 and the facilities were found to be in compliance with the Good Manufacturing Practice (GMP) Regulations.

This application was granted expedited review on May 2, 1994 because the use of this device for the stated indication has the potential for clinically meaningful increased public health benefit as an adjunct to mammography and/or physical examination of the female breast

XIII. APPROVAL SPECIFICATIONS

Directions for use: See attached labeling.

Conditions of approval: CDRH approval of this PMA is subject to full compliance with the conditions described in the approval order.

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that to ensure the safe and effective use of the device that the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii), (1) insofar as the labeling specify the requirements that apply to the training of practitioners who may use the device as approved in this order and (2) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

Warnings, Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, and Precautions in the attached labeling.

XIV. REFERENCES

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4. Charles E. Metz, "Basic Principles of ROC Analysis", *Seminars in Nuclear Medicine, Vol. VIII*, No.4. (Oct. 1978), pp. 283-298.

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4703-0026-03

Breast Lesion Sonography

Reference Manual

Rev C 4/11/96

29

Breast Lesion Sonography

Device Description

The device approved for this indication is an ATL (Advanced Technology Laboratories®; Bothell, Washington) Ultramark® 9 Ultrasound System with High Definition™ Imaging, using a broadband L10–5 linear array transducer. The system transmits ultrasound waves via the L10–5 transducer into a patient's breast, receives the echoes, and generates diagnostic images and Doppler information displays.

Indications and Usage

The ATL Ultramark® 9 Ultrasound System with High Definition™ Imaging (HDI®) with L10-5 scanhead is indicated as an adjunct to mammography and physical examination to provide a high degree of physician confidence in differentiating benign from malignant or suspicious breast lesions. This device provides the physician with additional information to guide a biopsy decision. Utility of this system has been demonstrated for lesions with an indeterminate Level of Suspicion (LOS 2–4) by conventional diagnostic modalities. Using the HDI system in the evaluation of solid mass characteristics can reduce the number of biopsies performed on indeterminate lesions.

CONTRAINDICATIONS:

None known.

WARNINGS:

The ATL-HDI Breast Protocol does not replace normal screening methods for breast disease by mammography or palpation and evaluation using biopsy when appropriate.

- *The mass seen on the ultrasound examination and the mass seen on the mammographic examination may not be the same mass; orientation must be carefully checked, especially when performing a biopsy on one of several lesions.*
- *If a mass cannot be visualized when attempting to follow the HDI protocol, then NO CHANGE IN PRIOR LEVELS OF SUSPICION SHOULD BE MADE.*
- *Overlap in ultrasound image appearance between benign and malignant breast lesions does exist.*

Precautions for Use

- The attending physician should determine the applicability of HDI results and the need for biopsy based upon individual patient characteristics and history.
- Training of Sonographers and Sonologists should take place prior to use of the HDI system for breast lesion differentiation. ATL will provide site training information and, in addition, will hold regional and national training programs. Please contact your ATL representative for this information.

This device has not been demonstrated effective for masses less than 1.0 cm, as measured by mammography.

- To ensure consistent operation, a semiannual quality check to verify system performance should be performed. Information regarding this program may be found in Section 2, Breast Lesions Quality Assurance Program, of this manual.
- To ensure optimal image evaluation there should be no prior surgical intervention of the breast, and at least two weeks healing should be allowed to occur following any percutaneous intervention to the breast.

Adverse Effects

During the clinical study, there were no reported adverse reactions or complications to study subjects due to the use of this device.

Possible adverse reactions to diagnostic ultrasound include:

- Dermal reaction to excessive temperature from the overheating of the lens face of the scanhead (reddening to burning of the skin) due to system control failure
- Tissue damage from excessive ultrasonic output (cavitational or thermal cell damage) due to system control failure
- Allergic reactions to the ultrasonic gel used to couple the scanhead to the skin

Patient Population

Based on the clinical results, HDI ultrasound should be used adjunctively with mammography or physical examination on women with:

- Any suspicious, indeterminate, or probably benign (LOS 2–4) lesion, seen as a discrete mass on HDI, in non-pregnant women.

Special Patient Population

Because no testing or analysis was done on certain patient populations in the ATL study, it is unknown whether information derived from HDI imaging of these populations would be useful in the decision process as to whether or not to biopsy the lesion. Therefore, clinical efficacy has not been demonstrated for:

- Men
- Women who are pregnant
- Women who have previously had breast cancer
- Women with mammary implants
- Lesions demonstrating classic mammographic features of a benign lesion and would not typically be biopsied in the given institution
- Mass size less than 1.0 cm.
- Breast lesions with previous surgery or needle intervention two weeks prior to ultrasound evaluation

Instructions for Use

All breast masses should be mammographically visualized and be indeterminate or suspected for malignancy by mammography, physical examination and/or conventional ultrasound (to rule out a simple cyst). These findings should be known at the time of the HDI exam. Clinical history, familial incidence of breast cancer and endocrine physiological status (i.e., lactation, menopausal, etc.) should be available. After the initial mammographic study, palpation and/or other diagnostic method has resulted in an indeterminate or suspicious finding, the patient may be referred for HDI sonography using the breast lesion protocol.

Sonographic Exam Protocol

The HDI sonographic breast lesion exam should be conducted by an experienced sonographer who has been trained in diagnostic breast imaging.

In general, HDI sonographic breast exams will include a complete gray scale and Doppler study of the suspected mass. Supplementary diagnostic information will be obtained by the assessment of blood flow characteristics associated with the mass using ultrasonic spectral and color Doppler techniques. The interpretative criteria developed from gray scale images and Doppler analysis will allow reliable detection and diagnosis of breast lesions.

One should use the software preset for breast applications as the default setting, and then adjust the preset values of the system controls during the study to optimize system diagnostic performance.

ATL notes that these guidelines are best applied to mammographically indeterminate cases. If the post-mammography level of suspicion is malignant (LOS 5), then there is little added value in the ultrasound study and it need not be performed. Similarly, if the diagnostic call based on mammography is definitely benign, it may not be cost effective to perform an ultrasound examination.

If a mass cannot be visualized when attempting to follow the HDI protocol, then NO CHANGE IN PRIOR LEVELS OF SUSPICION SHOULD BE MADE. For example, in a lesion demonstrating (mammographically) microcalcifications with no concomitant mass, HDI would fail to demonstrate any abnormal finding. Since this example lesion would be suspicious for DCIS, the failure of HDI to demonstrate a mass should not modify the mammographic level of suspicion.

Methodology

Differentiation of the breast lesion is made by evaluation of the patient history, pre-HDI examinations LOS (mammography and physical examination), HDI 2D LOS, and post-HDI Doppler LOS. The lesion's LOS may change throughout the different stages of the diagnostic evaluation based upon 2D or Doppler characteristics that match the benign or malignant criteria. The clinician must assess the cumulative diagnostic information in order to determine that the mass presents attributes that classify it as either malignant, benign, or indeterminate. Malignant and indeterminate cases should be sent to biopsy for confirmation of the diagnosis. Lesions diagnosed as benign after the HDI examination may be handled as benign lesions rather than biopsied. The attending physician should determine the applicability of HDI results and the need for biopsy based upon individual patient characteristics and history.

Preparation for the Breast Lesion Exam

Prepare the HDI system for a breast lesion sonography exam and enter the patient data as follows.

☐ **To select the L10-5 scanhead:**

1. Connect an L10-5 scanhead to one of the three scanhead receptacles.

NOTE: *See "Connecting Scanheads" in Section 3 for additional information on scanhead connection. See the "Transducer Select" section for additional information on scanhead selection.*

2. Press XDCR on the system control panel.
3. To select the L10-5 scanhead, press the *L10-5* selection on the *TRANSDUCER SELECT* panel.

☐ **To enter patient data:**

1. On the system keyboard, press PATIENT DATA.
2. In response to the EXAM prompt, press R (for radiology) on the keyboard.
3. Enter the remainder of the patient data, as required.
4. Press PATIENT DATA on the keyboard.

☐ **To select the breast exam preset:**

1. After entering patient data for a new patient, the RECALL sidebar for the exam type entered is displayed on the left video monitor.

NOTE: *If the RECALL sidebar is not displayed, press the SETUP button, and then, on the SETUP PANEL, press Recall Presets. For a complete description of application presets, see the "SETUP" section.*

2. Use the TRACKBALL to select BREAST from the RADIOLOGY RECALL sidebar.
3. Press SET to install the BREAST preset.
4. Press ENTER to quit the application preset selection function.
5. The system is now preset and ready for the BREAST exam.

2D Breast Imaging

NOTE: *For detailed instructions on acquiring a 2D image and using the HDI system controls to optimize the image, refer to the "2D" section.*

Prior to scanning, perform a supine physical examination of the patient. If the mass is palpable, locate it with your finger and the apply the ultrasound transducer to that area. Scan the entire quadrant in orthogonal projections, sagittal and transverse. Adjust the system settings at the outset to optimize imaging performance (gain compensation, gray scale curves, dynamic range, focal zone settings, etc.). Scan through the entire lesion in both projections. To visualize tissues deep to the nipple, place the transducer adjacent to the nipple and angle the sonic beam into the retroareolar area.

For studying the lateral upper quadrant, the patient shall generally be studied in the supine position. Ask the patient to position herself obliquely towards her contralateral side. The ipsilateral arm should be flexed, with the hand resting comfortably under the neck, and the torso supported by a wedge placed underneath. The patient should keep the contralateral arm at the her side. Completeness of the scan is assured if the underlying pectoral muscles and ribs are visualized.

For locations other than the upper quadrants, ask the patient to place her arms behind her head. If the mass or thickening is felt only when the patient is seated or standing, ask the patient to assume the appropriate position and pinpoint the site of concern with her fingers. Direct the scan to the area in question.

NOTE: *There is no need to use an offset gel pad with the HDI system utilizing the L10-5 scanhead.*

2D Characterization of Indeterminate or Suspicious Breast Lesions

Specific 2D mass characteristics should be assessed and recorded for each indeterminate lesion being evaluated. 2D LOS assignment and interpretation (page 1-6) is made from the following 2D lesion characteristics:

SHAPE - spherical, ovoid, lobulated, irregular

MARGIN DEFINITION - linear, poorly defined

TEXTURE - homogeneous, heterogeneous

ECHOGENICITY - isoechoic, anechoic

POSTERIOR SHADOWING - edge, central, none

POSTERIOR ENHANCEMENT - present, not present

ORIENTATION TO SKIN - parallel, not parallel

OTHER FEATURES - dilated duct, mobility, calcifications, architectural distortion

Detailed descriptions for these terms may be found in the teaching module (contact your ATL representative for this education program).

Doppler Examination

NOTE: *For detailed instructions on using the spectral and color Doppler functions, refer to the "Doppler" and "Color" sections of this manual.*

Color flow Doppler is used to identify and select blood vessels related to the mass for pulsed Doppler evaluation, and to assess vascularity of the contralateral breast region. For color flow Doppler, obtain data on the location of the flow in relation to the mass (i.e., internal, periphery, or other), and global variance and vascularity of the mass in relation to the same region of the contralateral breast. Both global variance and vascularity should be subjectively assessed in relation to the same region of the contralateral breast as less, same, or more.

The typical changes in flow patterns in the vicinity of a malignant lesion are a complex pattern of low-amplitude, high-frequency flow in the periphery of the lesion with a high-amplitude, high-frequency component due to arteriovenous shunts. Scan the region of interest slowly using light scanning pressure. Using angle correction (when possible) obtain peak velocity from the most obvious vessel and record it for comparison to known normal blood flow velocities in these vessels. For the pulsed Doppler exam, peak velocity, Resistive Index, and Pulsatility Index data should be obtained for blood flow from the most prominent vessel associated with the mass. Similar data should also be collected from the same region of the contralateral breast to establish the patient's normal hemodynamic characteristics. Record all settings and videotape imaging studies for further review off-line.

Doppler and Color Flow Characterization of Indeterminate Breast Lesions

Specific Doppler and Color flow attributes should be assessed and recorded for both the affected and contralateral breast. Doppler LOS assignment and interpretation (page 1-6) is cumulatively assigned after evaluating the following Doppler and Color flow characteristics:

GLOBAL VARIANCE - affected breast has more or less vessel tortuousity than contralateral side

VASCULARITY - affected breast has more or less vascularization than contralateral side

Interpretation of Results

The recommended criteria are based on a retrospective analysis of all patients enrolled in the clinical study. All criteria resulting in a true (diagnosis of imaging and pathology identical) biopsy yield of 65% or greater were included in the criteria list.

2D Image Criteria Guidelines for Differentiation of Breast Lesions

Image Criteria Associated with Benign Lesions

1. Spherical/ovoid/lobulated shape
2. Linear margin
3. Homogeneous texture
4. Isoechoic/anechoic
5. Edge shadow
6. Parallel to the skin
7. Distal enhancement
8. Dilated duct/mobile

Image Criteria Associated with Malignant Lesions

1. Irregular shape
2. Poorly defined margin
3. Central shadowing
4. Distorted architecture
5. Calcifications
6. Skin thickening

The LOS should be based on the following guidelines.

Table 1-1. 2D Image LOS Guidelines

LOS	Diagnosis	Number of Criteria
5	malignant	5 malignant criteria
4	probably malignant	3–4 malignant criteria
3	indeterminate	1–2 malignant criteria
2	probably benign	0 malignant criteria
1	benign	0 malignant criteria & all benign criteria

Based on the final overall level of suspicion from both the HDI protocol and other previous conventional modalities, the attending physician should determine the applicability of HDI results and the need for biopsy based upon individual patient characteristics and history.

Doppler Criteria Guidelines for Differentiation of Breast Lesions

The results for pulsed and color flow Doppler show that there is a statistically significant difference when either a benign or malignant mass is present when compared to the contralateral side.

The clinical study results for color flow Doppler show that masses that exhibit the same or less global variance or vascularity as the same region of the contralateral breast should be subjectively interpreted as an indicator of a benign lesion.

Overall, the peak mean velocities of malignant lesions were higher than those for benign masses or from the contralateral side. However, the wide variation of peak velocities in the study population did not allow for a statistical separation of benign from malignant masses based on peak velocities alone.

In addition to the 2D imaging criteria, the Doppler attributes that can be used to help differentiate a mass as benign or malignant are as follows.

Benign Doppler Criteria

1. Same or less global variance when compared to the contralateral breast.

2. Same or less vascularity when compared to the contralateral breast.

Malignant Doppler Criteria

1. More global variance when compared to the contralateral breast.

2. More vascularity when compared to the contralateral breast.

Results of Clinical Studies

ATL® conducted a multi-site study to investigate the clinical utility of the Ultramark® 9 system with the High Definition Imaging (HDI®) technology and the L10-5 scanhead as an adjunct to mammography and physical examination for the differentiation of benign and malignant breast lesions. The study was conducted according to ATL Clinical Protocol #1075, which was designed to obtain diagnostic ultrasound images and physiological data from the study subjects. The only hypothesis of the study was related to an increase in specificity, with an assumption of at least an equivalent level of sensitivity.

The protocol used historic controls based upon available data from each of the 14 institutions participating in the study. In addition, there is a comparative control designed into the study in that the radiological diagnosis for each subject is compared to the pathology biopsy results, which are considered to be the "gold standard" for diagnostic and statistical purposes.

Each of the study subjects had a mammographic and/or physical examination with a finding suspicious for malignancy which resulted in a recommendation for biopsy. This clinical data and patient status were known at the time of the ultrasound examination and correlated with sonography.

A Patient Questionnaire was filled out by the subject, and includes demographic data, gynecological information, family incidence of breast cancer, and clinical status and history.

Investigators scored the level of suspicion (LOS) of the mass three times for each study subject:

- Pre-HDI LOS: after the mammography, palpation, and/or conventional ultrasound (cyst vs. solid) work-up
- HDI 2D LOS: after the 2D image study
- Post-HDI LOS: after the pulsed and color Doppler exam

A scale of 1 to 5 was used for each LOS score with a larger number indicating a greater suspicion of malignancy. These numeric scores were not considered to be definitive, although they were intended to be interpreted within the following guideline: (1) benign, (2) probably benign, (3) indeterminate, (4) probably malignant, and (5) malignant. Each LOS score was based upon all previous clinical information and earlier LOS(s), thereby replicating clinical practice which relies upon cumulative knowledge.

A final diagnosis was made at the conclusion of the HDI exam when the investigator indicated that the mass was either malignant, benign or indeterminate. After the biopsy procedure, the pathology report was obtained and data from it was used to complete the DF.

Effectiveness of the Device for the Study Protocol

HDI ultrasound proved to be statistically significantly useful when evaluating suspect masses with a pre-HDI LOS of 2, 3, or 4. For comparison of indeterminate masses, the statistical analysis involved 431 suspect masses, of which 99 masses were determined to be malignant through biopsy. The primary statistical analytic technique was receiver operating characteristic (ROC) which compared the diagnostic accuracy of the modalities studied. This analysis focused on a comparison of:

- Mammography and/or physical examination alone versus those results plus HDI 2D imaging and HDI Doppler (post-HDI Doppler)

The indices analyzed were:

- Area under the ROC curve
- Sensitivity at specificity = 0.85
- Sensitivity at specificity = 0.60

Table 1-2. ROC Comparison of pre-HDI to Post-HDI Doppler Results for Indeterminate Lesions

ROC Index	Pre-HDI	Post-HDI Doppler	P-value
Area under the ROC curve	0.850	0.920	0.0024
Sensitivity at specificity = 0.85	0.664	0.828	0.0037
Sensitivity at specificity = 0.60	0.890	0.970	0.0098

These results showed increased accuracy which were statistically significant for all ROC indices post-HDI Doppler.

For indeterminate masses seen on the HDI system, the performance parameter results based on the final physician's call were:

Performance Parameter	Post-HDI Doppler
Sensitivity	100.0
Specificity	53.0
PPV	38.8
NPV	100.0

The use of these criteria in the indeterminate cases from this study would have resulted in a 40.8% reduction in biopsies. Despite this, overlap in ultrasound image appearance between benign and malignant breast lesions does exist.

Other considerations in determining the effectiveness of the device involve the false negative and false positive results of the study.

Conclusion

The clinical investigation conducted on the HDI system demonstrated that HDI technology provides physicians a high degree of confidence in differentiating benign from malignant breast lesions when used as an adjunct to mammography and physical exam than do mammography and physical exam alone.

Safety of the Device for the Study Protocol

Precautions taken prior to the initiation of the clinical study included nonclinical biocompatibility testing of the parts of the L10-5 scanhead that come into contact with patients. The equipment materials passed all biocompatibility tests to which they were subjected. Other safety testing for potential effects that would affect the operator as well as the patient included electrical current leakage testing. There were no reports of adverse effects, such as electric shock from any of the operators of the equipment. Moreover, there were no reports on dermal reactions, tissue damage or allergic reactions, on any patient.

There were no unique diagnostic ultrasound safety considerations as part of the clinical protocol. The HDI system and L10-5 scanhead were used in a manner consistent with general purpose diagnostic ultrasound exams with respect to scanning techniques, acoustic output exposure levels, and duration's of exposure. What was unique about the protocol was the diagnostic interpretation of the images obtained during the study, not the exam procedures nor system operation.

Breast Lesion Quality Assurance Program

In order to verify the HDI system performance is adequate to conduct the Breast Lesion Protocol, the following quality tests (Sections 3 and 4) should be conducted. The recommended tests may be performed by the system operatior, in-house biomedical engineers, or your ATL Customer Service Representative. The tests are both quantitative and qualitative and they assess the image quality of the HDI system when configured with the L10-5 scanhead for breast examinations.

The tests should be conducted minimally every six months or whenever a suspected problem has developed. Physical examination of the L10-5 scanhead should be made on a daily basis to inspect for any visible damage or wear to the scanhead lens, shell casing or cable. Should any problems with the system or scanhead develop, please contact ATL Customer Service for assistance.

A checklist is provided for your use (Section 5).

Quantitative Tests

2D Resolution

Equipment Setup

Use an RMI 413/403 or equivalent test phantom for the following test.

NOTE: *All items of test equipment which require routine calibrations shall be calibrated and certified. The user is responsible for ensuring that the test equipment they use for these tests is not overdue for calibration and certification.*

2D Resolution Test Procedure

☐ **To set up the system:**

1. Make the following system parameter changes:

Mode:	2D only
Depth:	4 cm
Output:	Default
TGC:	Adjust so the nylon targets of the phantom are clearly distinguished from the back scatter echoes.
NOTE:	Best to start at center of setting.
Application:	Small Parts/Breast
Line Density:	Maximum
#Focal Zones:	1
Focal Depth:	2 cm
2D Dynamic Range:	40 dB
2D Map:	6
Output:	Default
Frame Rate:	Adjust to remove reverb artifacts

2. Press setup key.
3. On the setup panel, press the non-outlined key (to the right of change status) 4 times quickly.
4. Select test patterns from the Production-Service test panel.
5. Select Resolution Test Key.
6. Select return on each test panel until you get back to 2D Controls.

☐ **To begin the test:**

1. Obtain a 2D phantom image of the pin at the 2 cm depth.
2. Ensure the ultrasound scanning plane is perpendicular to the pin by turning the probe left and right and forward and back along the axis of the probe.

NOTE: *Depending on the phantom and the pin used, it may be difficult to see the pin until zoomed.*

3. Adjust so the pin can be viewed with maximum width on the sector edge.
4. Zoom the image to the maximum amount.
5. Adjust the trackball as needed to ensure that the selected pin remains in view.

NOTE: *Currently only the 0 dB and the -20 dB contour are used for verification. The -6 dB contour line is used for data gathering and special testing only.*

NOTE: *The axial resolution is the measured height. The lateral resolution is the measured width.*

6. Fine adjust the scanhead position to obtain best image.

NOTE: *For best results, center the pin in the middle of scanplane.*

7. Adjust the TGC and 2D Gain so that the center of the pin contains a small dot (0 dB) with the outline of the pin highlighted with a line at -20 dB contour line.

8. Freeze the image.

9. Using the 2D distance cursors, measure the height and width at the -20 dB contour line of the pin. (See **Figure 3-1.**)

10. Record the results.

11. Ensure the test passed by comparing the recorded results to the expected results listed in the checklist.

❑ **To return system to standard imaging:**

1. Press Zoom Off (2D Controls).

2. Repeat steps 2 - 6 of **To set up the system.**

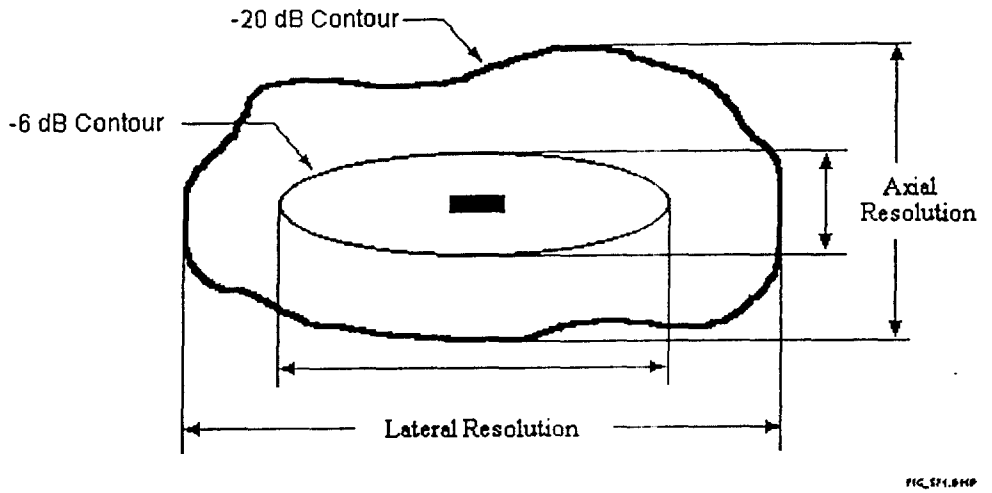


Figure 3-1. Scanhead Resolution

2D Penetration

Equipment Setup

Use an RMI 413/403 or equivalent test phantom for the following test.

NOTE: *All items of test equipment which require routine calibrations shall be calibrated and certified. The user is responsible for ensuring that the test equipment they use for tests is not overdue for calibration and certification.*

2D Penetration Test Procedure

☐ **To set up the system:**

1. Make the following system parameter changes:

Scanhead:	L10-5
Application:	Small Parts/Breast
Mode:	M-Mode scrolling

☐ **To measure scanhead penetration:**

1. Press setup key.
2. On the setup panel, press the non-outlined key (to the right of change status) 4 times quickly.
3. Select OFE test.
4. Couple the scanhead to the RMI phantom and scan an area containing no pins or cysts (i.e. straight down through homogeneous phantom tissue).
5. Select 2D penetration.

NOTE: *The 2D penetration will be displayed on the left monitor.*

6. Record the results.
7. Press return on each panel until you return to M-Mode controls.
8. Ensure the test passed by comparing the recorded results to the expected results listed in the checklist.

☐ **To return to standard imaging:**

1. Press Return on the Control Panel until you reach M-Mode Controls.

Registration Accuracy

2. Couple a probe to the RMI phantom and obtain an image that clearly shows both the horizontal and the vertical rows of pins.
3. Position the probe so that a horizontal row of pins at 3 cm apart and a vertical column at 2 cm apart can be seen, ensuring that the scanning plane is perpendicular to the pins. Adjust TGC, Power, and Gain so all pins can be viewed, with each pin indicating maximum width on the sector image.
4. Press the FRZ button to freeze the image.
5. Press the CALC button on the front panel.
6. Measure the distance between any two pins in the vertical column that are spaced 2 cm apart and any two pins in the horizontal row that are 3 cm apart.
   a. Use the trackball to position the cursor to the measurement start point. Place the cursor in the center of the pins.
   b. Press the SET button.
   c. Use the trackball to position the cursor to the measurement end point. Place the cursor in the center of the pins.
   d. Press the ENTER button on the front panel to fix the measurement.
7. Record the results.
8. Ensure the distance measured meets the expected tolerances listed in the checklist.

Qualitative Tests

2D Imaging

Couple the scanhead to a phantom and verify the T.G.C., depth, and power controls can be adjusted to produce a smooth and uniform image. Verify the absence of any imaging artifacts or abnormalities.

The production of a quality image can be expressed as the accurate portrayal of:

- Size
- Shape
- Position
- Tissue

The criteria used in assessing a quality image are:

- Uniform ray formation and distribution
- Like tissues look alike, unlike tissue look different
- It is possible to "write to white", (use all gray shades)
- Cystic structures look cystic
- Solid structures look solid
- Enhancement behind low attenuators
- Shadowing behind high attenuators

Record any abnormalities.

Image Uniformity/Vertical Uniformity

☐ **To set up the system:**

1. Make the following system parameter changes:

Select:	L10-5
Application:	Small Parts/ Breast
Depth:	4 cm
Curve:	6
Focal Zones:	All On
Dynamic Contrast Enhancement:	Off
Dynamic Range:	50 dB

☐ **To begin the test:**

1. Couple the scanhead to the RMI phantom and scan an area containing no pins or cysts (i.e. straight down through homogeneous phantom tissue).
2. Adjust output to one step below 50%.
3. Adjust TGC and Gain to obtain a uniform image that is not saturated.
4. Freeze image.
5. Check for image uniformity:

   Horizontally: Check image for uniform brightness in the horizontal plane. Record any inconsistencies found.

   NOTE: *Uniformities/consistency problems in the horizontal plane are most likely to occur between focal zones.*

   Vertically: Check image for uniform brightness in the vertical plane. Also check for any banding in the vertical plane. Verify that image near the edges are the same intensity as the middle. Record any inconsistencies found.

   NOTE: *Uniformities/consistency problems in the vertical plane are most likely hardware related like bad elements in the scanhead or channel board failure.*

6. Unfreeze the image.

Clutter in Cystic Structure

1. Set dynamic range to 60 dB
2. Set the output just below midrange setting
3. Set the TGC to obtain the optimal image
4. Turn on all transmit focal zones
5. Dynamic Contrast Enhancement - Off

The cystic structure at the focal zone should be echo-free, round, and with sharp walls at levels corresponding to focal zones. With the image in the defaulted depth setting and the image zoomed, some slight fuzziness is acceptable.

Video Monitor Setup

The following procedure is used not only to setup the monitors for optimal viewing, but also to check the range of contrast and brightness of the monitors. Linearity is also tested.

1. Press Setup key.
2. On the setup panel, press the non-outlined key (to the right of change status) 4 times quickly.
3. Select test patterns from the Production–Service test panel.
4. Press VIDEO PR TEST.
5. On the VIDEO PROCESSOR TEST panel, press GRAY SHADES.
6. On both monitors set BRIGHTNESS fully counterclockwise and rotate CONTRAST fully counterclockwise. Verify that the video display has a flat black appearance.
7. Rotate CONTRAST fully clockwise. On the monochrome monitor, verify that the white parts of the video display bloom. On the color monitor, verify that the level of contrast varies.
8. Readjust CONTRAST for correct contrast (i.e., sixteen grayshades and no blooming).
9. On the monochrome monitor, rotate BRIGHTNESS fully counterclockwise. Verify that the video display becomes completely dark. (If it does not, then adjust CONTRAST slightly counterclockwise until it does.)
10. On the monochrome monitor, rotate BRIGHTNESS fully clockwise. Verify that the video display is washed out (there appears to be relatively little contrast).
11. With the room lighting set to normal scanning conditions, readjust BRIGHTNESS and CONTRAST controls for customer approval and the best image:
    a. sixteen grayshades
    b. no blooming
    c. black grayshade almost blends with background
12. Press MONITOR BALANCE, and verify that a black background with a white rectangle in the center is displayed on both monitors (monochrome and color), and that both monitors are approximately equal in appearance with respect to black and white values.
13. Press FLAT BLACK. Verify the following:
    a. The color monitor matches the monochrome monitor with respect to color (grayness) and intensity.
    b. The grayness of the color monitor display is not tinted with another color (i.e., reddish brown, blue, or green).
14. Press CROSS HATCH. Verify the following:
    a. On NTSC systems, the crosshatch pattern appears centered vertically and horizontally. On PAL systems, the crosshatch pattern is centered horizontally and occupies the top three-fourths of the display (a blank area is displayed at the bottom).
    b. The horizontal and vertical lines appear straight (within ± 0.5 mm).
    c. All of the boxes appear to be about the same size
15. Press COLORBAR RGB. Verify the following:
    a. A color test pattern appears on the color monitor.
    b. The colors are arranged as follows from left to right across the video display: white, yellow, light blue, green, violet, red, dark blue.
    c. Each individual color appears vivid and uniform.
16. Return to 2D CONTROLS.
17. Use the measurement calipers and measure the image width.
18. Record the result.

Multi-Image Camera Tests

NOTE: *This procedure covers both the Matrix and Aspect cameras.*

1. Press SETUP, and then press HARDCOPY CONTROLS.

2. Prepare the camera for operation as follows:

   a. Insert a loaded film cassette.

   b. Remove the dark slide.

   c. Verify that the camera pulls the cassette into position (Matrix only).

   d. Display the test sector on the right monitor.

   e. Press STARTING LEVELS for the camera settings.

3. Press PRINT R on the UM-9 HDI control panel to select the right monitor.

4. Press SETTINGS AND STATUS. Use the trackball to select a group of brightness, contrast, and exposure settings. Use the gain controls to vary the levels of brightness, contrast, and exposure time (directions are displayed on the monitor).

5. Take the remaining prints of the Test Sector. Ensure that three of the remaining prints are taken in negative image, that the PRINT footswitch works properly, and that PRINT L button works properly.

6. Use the settings already established, or change them as desired. Press PRINT 6 FOR REVIEW, and verify the following:

   a. Six exposures are taken that correspond to the SETTINGS in the SETTINGS matrix.

   b. During each exposure the indicators for the selected monitor, FRZ, and PRINT are ON.

   c. The camera shutter makes a clicking sound (Matrix only).

   d. The cassette position motor runs every second exposure (Matrix only).

   e. After the last exposure, LAST FRAME EXPOSED is displayed on the monitor.

   f. Verify the cassette is ejected (Matrix only).

7. Develop the film, and verify the following:

   a. The graphics on the print are clear, legible, and accurately represented.

   b. The graybar test pattern and the TGC curve are accurately represented.

   c. Contrast and brightness variations between exposures.

   d. Absence of light leaks.

   e. Absence of speckles on the image (due to dirty optics).

   f. Absence of dark bands.

   g. Presence of 16 shades of gray in Test Sector images.

   h. Sector images are 90° ± 1° measured with a sector overlay using the following materials:

      CSR Tool Kit (193-90003-01)

      RMI Model 413 Tissue Equivalent Phantom (199-12204-00)

      UM-9 Monitor Overlay (4100-0890-01)

   i. Sector image edges are not bowed more than 1.5 mm. (Scanlines on outside edge of the sector are not deflected more than 1.5 mm.)

   j. The four sides of the prints do not display evidence of edge blanking.

8. If the exposures are not acceptable, insert another film cassette, change the brightness, contrast, and exposure settings, and take six more exposures. Take three exposures in standard video and three in negative image.

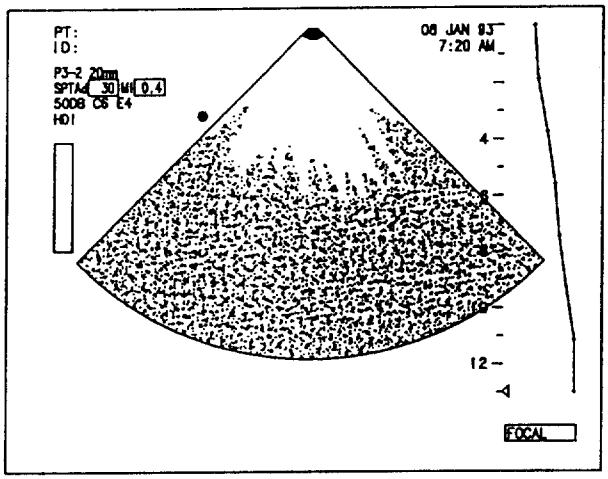
9. If the camera does not work properly, refer to the camera service manual.

2D Tests

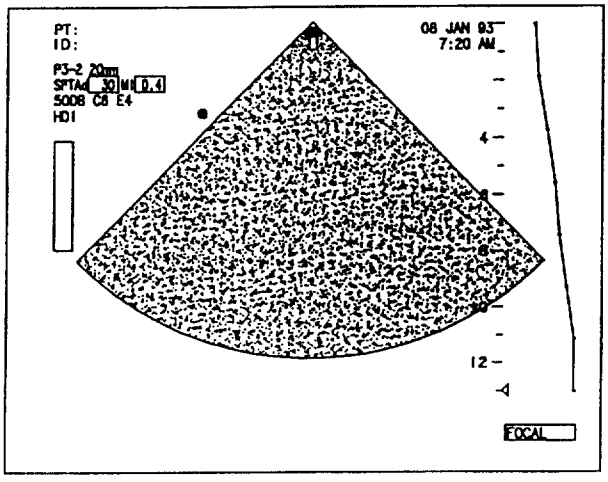
Gain, Output, and Depth

1. Press the 2D button, if necessary, to select 2D mode, and obtain a phantom image.

2. Rotate the 2D/M GAIN control through its full range of motion, and verify that the number of echoes in the image varies (**Figure 2-1**).



– LOW GAIN –



– HIGH GAIN –

Figure 2-1. Gain Range

3. Move each SLIDEPOT through its full range of motion and verify that the slope of the line segment associated with each SLIDEPOT responds. Also verify that the image display responds to the change in TGC in the region that is associated with the respective SLIDEPOT (**Figure 2-2**).

NOTE: *Some linear array scanheads will not be affected by movement of the first two slidepots.*

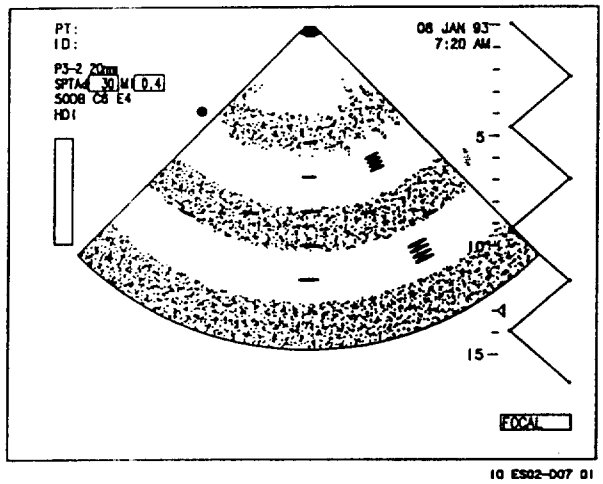


Figure 2-2. Slidepot TGC Variation

4. Rotate the OUTPUT rotary control counterclockwise to set SPTAd to 0.0, and verify that the image contains no echo information. Also verify that at the extreme counterclockwise setting an audible click is emitted from the control panel speaker. (If the TGC slidepots are full left, there will be no noise in the sector; if the TGC slidepots are not full left, there will be noise in the sector.)

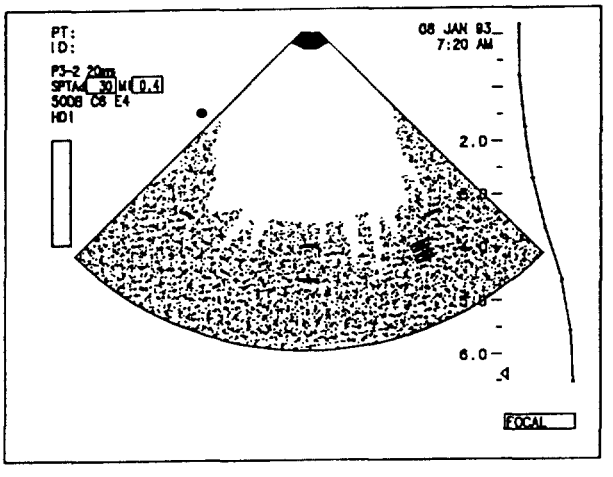
5. Rotating the OUTPUT rotary control clockwise, verify that the SPTAd value increases in discrete steps. Verify that at the extreme clockwise setting an audible click is emitted from the control panel speaker.

6. Rotate the DEPTH rotary control (**Figure 2–3**). Verify the following:

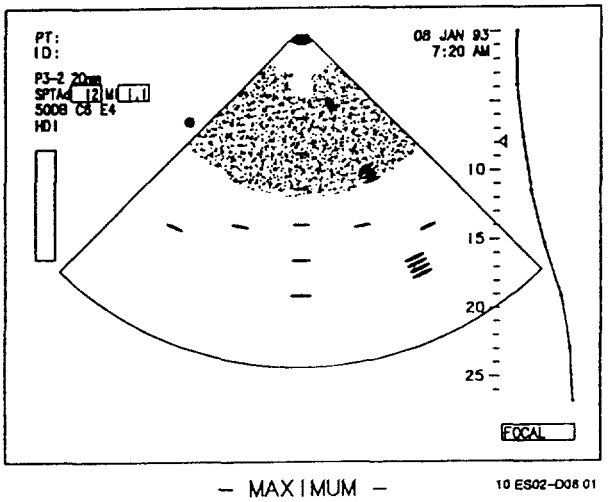
   a. Depth markers change to reflect the change in DEPTH setting.

   b. Image frame rate (FR # HZ) increases or decreases as DEPTH limit decreases or increases (press LINE DENSITY, if necessary, to display FR annotation).

   c. At the extreme DEPTH settings an audible clicking is emitted from the speaker.



– MINIMUM –



– MAXIMUM –

10 ES02-006 01

Figure 2–3. Depth Range

7. Press IMAGE PROCESS. Verify the following:

   a. Each processing curve changes the grayscale assignment of the image and the graybar.

   b. Display annotation is updated accordingly.

   c. The processing curves can be changed in live or freeze.

8. Select processing curve 3.

9. Press DYNAMIC CONTRAST ENHANCEMENT. Verify the following:

   a. As the level of enhancement is increased from E0 through E7, the phantom image becomes smoother and that low to mid-level echoes move in slow motion in response to scanhead movement or depth changes.

   b. High level echoes are updated faster, but also fade out in slow motion.

   c. Any slight scanhead shimmer or far field noise is averaged out.

10. Select enhancement level E0.

11. Press DYNAMIC RANGE. Verify the following:

   a. Dynamic range changes from 35 dB to 60 dB in 5 dB steps.

   b. Dynamic range cannot be changed in freeze.

   c. A high dynamic range causes the scatter echoes to smooth out in grayshade.

   d. The pins in the phantom appear at a lower echo level (the echoes are not as bright) at higher dynamic ranges.

Physical Inspection of Scanhead

1. Inspect the scanhead and cables daily for any damage as follows:
   - Visually inspect cables for cuts, exposed wires, and shielding damage.
   - Inspect scanhead for cracks, splitting, deformities, or delamination* of the transducer.
   - Inspect transducer lens for cuts, excessive wear, and uniformity.

   If any of the above problems are found, discontinue use of the scanhead.

* Delamination may be detected by applying light finger tip pressure and running your finger down the face of the scanhead and visually inspecting the lens material for bubbles or wrinkles. The 2D image may also demonstrate "dropout" with an uncoupled scanhead in the area of the delamination.

Reference

Madsen, Ernest L., Ph.D.; Garra, Brian S., M.D.; Parks, John A., B.A., R.D.M.S.; Skelly, Andrea C., B.S., R.D.M.S., R.D.C.S.; Zagzebski, James A., Ph.D.; *AIUM Quality Assurance Manual for Gray-Scale Ultrasound Scanners - Stage 2*, American Institute of Ultrasound in Medicine, 1995.

Quality Assurance Checklist

Name: _____
Date: _____
Scanhead Serial #: _____
Phantom Serial #: _____

System Serial #: _____
Build Version: _____
System Type: _____
Date last calibrated: _____

1 Quantitative Test Results

2D Resolution Test results	Measured	Expected
2D Axial resolution (mm)	_____	≤ 1.2 mm
2D Lateral resolution (mm)	_____	≤ 1.2 mm

2D Phantom results	Phantom Error	Measured	Expected
2D Penetration	_____	_____	≥ 4.8 cm

Registration Accuracy results	Measured	Expected
Vertical	_____	2.0 ± 0.15 cm
Horizontal	_____	3.0 ± 0.15 cm

2 Qualitative Test Results

2D Imaging

Abnormalities: _____

_____

Image Uniformity/Vertical Uniformity

Horizontal inconsistencies: _____

_____

Vertical inconsistencies: _____

_____

Clutter in Cystic Structure

Horizontal inconsistencies: _____

_____

Video Monitor Setup Results	Pass	Fail	Comments
Contrast	_____	_____	_____
Brightness	_____	_____	_____
Monitor balance	_____	_____	_____
Flat black	_____	_____	_____
Crosshatch	_____	_____	_____
Color RGB	_____	_____	_____

	Measured	Expected
Image width	_____	38.4 ± 0.1 cm

Multi-Image Camera Test results

	Pass	Fail	Comments
Print R			
Print L			
Footswitch			
Graphics			
Graybar pattern			
TGC			
Contrast			
Brightness			
Light leaks			
Image optics			
Dark bands			
16 gray levels			
Camera			

Gain, Output, and Depth results

	Pass	Fail	Comments
Gain			
Slidepot			
TGC			
Output			
Depth			
Image curve			
DCE			
Dynamic Range			

Physical Inspection of Scanhead

	Pass	Fail	Comments
Scanhead inspection			

50